

73633

SEARCH REQUEST FORM

127723

Requestor's

Name: DAVE NGUYEN

JUL 21 2004

Serial

Number: 101089, 312Date: 7/16/04Phone: 514-272-0731Art Unit: 1632

2031 2018 1101

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search claim 21, wherein the zwitterionic phospholipid comprises $R^3COOCCH_2CH(COCOR^4)CH_2OPO(OH)_2$, which is linked to an alkane diyl-containing moiety 5 and wherein the cationic compound has the formula as set forth in claim 22.

Claim Sheet is attached

for specific Thanks

Date Nguyen

Reason 2D31

Mail Box 2C18

STAFF USE ONLY

Date completed: _____

Search Site

Vendors

Searcher: _____

 STIC IG

Terminal time: _____

 CM-11068.94

STN

Elapsed time: _____

 Pre-S Dialog

CPU time: _____

 N.A. Sequence APSTotal time: 1 30 A.A. Sequence GeninfoNumber of Searches: 48 Structure SDC

Number of Databases: _____

 Bibliographic DARC/Questel Other



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 127723

TO: Dave Nguyen
Location: rem/2d31/2c18
Art Unit: 1632
Thursday, July 29, 2004
Case Serial Number: 10/089312

From: Paul Schulwitz
Location: Biotech-Chem Library
REM-1A65
Phone: (571)272-2527
paul.schulwitz@uspto.gov

Search Notes

Examiner Nguyen,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2527



STIC SEARCH RESULT FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact:*

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedback Form

➤ *I am an examiner in Workgroup:* Example: 1610

➤ *Relevant prior art found, search results used as follows:*

- 102 rejection
- 103 rejection
- Cited as being of interest
- Helped examiner better understand the invention
- Helped examiner better understand the state of the art in their technology

Types of relevant prior art found:

- Foreign Patent(s)
- Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ *Relevant prior art not found:*

- Results verified the lack of relevant prior art (helped determine patentability)
- Results were not useful in determining patentability or understanding the invention

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.



Inventors

Nguyen 10/089,312

07/29/2004

L5 ANSWER 1 OF 1 HCPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2001:265230 HCPLUS
 DOCUMENT NUMBER: 134:285563
 ENTRY DATE: Entered STN: 13 Apr 2001
 TITLE: Liposome-entrapped DNA oral
 vaccines
 INVENTOR(S): Gregoriadis, Gregory; Perrie, Yvonne
 PATENT ASSIGNEE(S): Lipoxen Limited, UK
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: A61K009-127
 SECONDARY: A61K048-00; C12N015-88
 CLASSIFICATION: 63-3 (Pharmaceuticals)
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024773	A1	20010412	WO 2000-GB3773	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1217989	A1	20020703	EP 2000-964471	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003529550	T2	20031007	JP 2001-527772	20001002
PRIORITY APPLN. INFO.:			EP 1999-307786	A 19991001
			WO 2000-GB3773	W 20001002

OTHER SOURCE(S): MARPAT 134:285563

ABSTRACT:

An oral vaccine comprises liposomes and complexed or, preferably, entrapped DNA operatively encoding an antigen, in which the liposomes are formed from components including cationic compds. and zwitterionic phospholipids. The hydrophobic groups within the liposome forming compds. must include at least one group which is saturated. This is believed to raise the transition temperature, rendering the liposomes more stable when delivered orally. The compns. have been found to give detectable increased in IgA levels, secreted Ig's of importance in efficacious oral vaccine delivery. Liposomes comprising phosphatidylcholine 32, dioleoyl phosphatidylethanolamine 16, and dioleoyl trimethylammonium propane 8 μ moles were prepared using the dehydration-rehydration method. PRc/CMV HBS plasmid DNA encoding for the small region of hepatitis B surface antigen was entrapped in the above liposome formulations. Entrapment complexation efficiency was 85-95%. Immunization of mice with the liposomes is described.

SUPPL. TERM: liposome phospholipid DNA oral vaccine
 INDEX TERM: Lipids, biological studies

INDEX TERM: ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycerolipids; liposome-entrapped DNA oral vaccines)

INDEX TERM: Freeze drying
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Antigens

DNA

Nucleic acids

ROLE: BAC (Biological activity or effector, except adverse);
BSU (Biological study, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Phosphatidylcholines, biological studies

INDEX TERM: Polynucleotides

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Drug delivery systems
(liposomes; liposome-entrapped DNA oral vaccines)

INDEX TERM: Vaccines
(oral; liposome-entrapped DNA oral vaccines)

INDEX TERM: Drying
(spray; liposome-entrapped DNA oral vaccines)

INDEX TERM: Phospholipids, biological studies

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zwitterionic; liposome-entrapped DNA oral vaccines)

INDEX TERM: 57-88-5, Cholesterol, biological studies 2462-63-7,
Dioleoyl phosphatidylethanolamine 2644-64-6,
Dipalmitoylphosphatidylcholine 4537-76-2,
Distearoylphosphatidylethanolamine 4539-70-2,
Distearoylphosphatidylcholine 5681-36-7,
Dipalmitoylphosphatidylethanolamine 113669-21-9
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

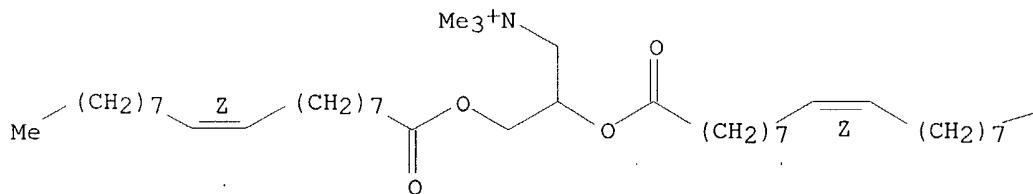
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Gregoriadis, G; WO 9810748 A 1998 HCPLUS
(2) Gregoriadis, G; Febs Letters 1997, V402(2/03), P107
(3) Gregoriadis, G; Methods 1999, V19(1), P156 HCPLUS
(4) Han, M; Journal of Veterinary Medical Science 1997,
V59(12), P1109 HCPLUS
(5) Perrie, Y; British Pharmaceutical Conference 1998,
V50(Suppl), P103

L6 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **113669-21-9** REGISTRY
 CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-
 (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-,
 (Z,Z)-
 FS STEREOSEARCH
 MF C42 H80 N O4
 CI COM
 SR CA
 LC STN Files: CA, CANCERLIT, CAPLUS, IPA, MEDLINE, PROMT, TOXCENTER,
 USPAT2, USPATFULL
 DT.CA CAplus document type: Conference; Journal; Patent
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
 PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
 study); USES (Uses)
 RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
 study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC
 (Process); PRP (Properties); USES (Uses)
 RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
 study); FORM (Formation, nonpreparative); PREP (Preparation); PRP
 (Properties); USES (Uses)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

71 REFERENCES IN FILE CA (1907 TO DATE)
 5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 71 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
 RN **5681-36-7** REGISTRY
 CN Hexadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-
 ethanediyl ester (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:

CN Ethanol, 2-amino-, dihydrogen-phosphate (ester), monoester with 1,2-dipalmitin, DL- (8CI)
 CN Hexadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester, (±)-
 CN Palmitin, 1,2-di-, 2-aminoethyl hydrogen phosphate, DL- (8CI)
 CN Palmitin, 1,2-di-, phosphate, 2-aminoethyl ester, dl- (6CI)

OTHER NAMES:

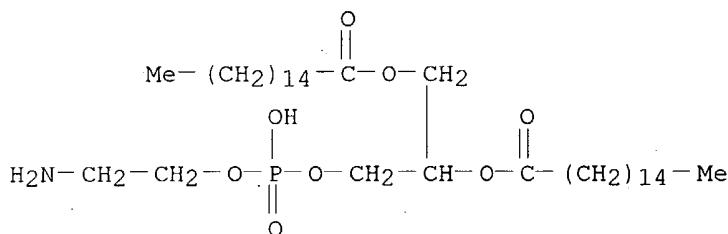
CN α -Cephalin, β,γ -dipalmitoyl-
 CN β,γ -Dipalmitoyl-DL- α -cephalin
 CN 1,2-Dipalmitoyl glycerylphosphorylethanolamine
 CN 1,2-Dipalmitoyl-3-DL-glycerylphosphorylethanolamine
 CN 1,2-Dipalmitoyl-DL-3-glycerophosphatidylethanolamine
 CN 1,2-Dipalmitoyl-DL-phosphatidylethanolamine
 CN 1,2-Dipalmitoyl-rac-glycerophosphoethanolamine
 CN 1,2-Dipalmitoylphosphatidylethanolamine
 CN Dipalmitoyl cephalin
 CN Dipalmitoylphosphatidylethanolamine
 CN DL- α -Cephalin dipalmitate
 CN DL- α -Dipalmitoylphosphatidylethanolamine
 CN DL-Dipalmitoylphosphatidylethanolamine
 CN DPPE
 FS 3D CONCORD
 DR 3026-45-7
 MF C37 H74 N O8 P
 CI COM

LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, IPA, MEDLINE, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL
 (*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA CAplus document type: Conference; Journal; Patent; Report
 RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
 RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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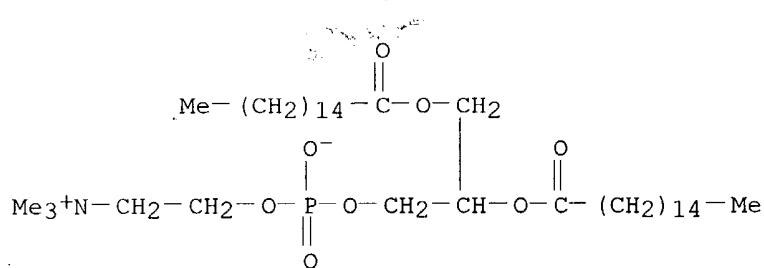
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1004 REFERENCES IN FILE CA (1907 TO DATE)
 132 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1006 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 4539-70-2 REGISTRY
 CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Choline phosphate, 3-ester with 1,2-distearin (6CI)
 CN Choline, hydroxide, dihydrogen phosphate, inner salt, ester with 1,2-distearin (8CI)
 OTHER NAMES:
 CN (±)-1,2-Distearoylglycero-3-phosphorylcholine
 CN β , γ -Distearoylphosphatidylcholine
 CN 1,2-Dioctadecanoyl-rac-glycerol-3-phosphorylcholine
 CN 1,2-Distearoyl-3-glycerophosphorylcholine
 CN 1,2-Distearoyl-DL-phosphatidylcholine
 CN 1,2-Distearoylglycerol-3-phosphorylcholine
 CN 1,2-Distearoylglyceryl 3-phosphorylcholine
 CN 1,2-Distearoyllecithin
 CN Coatsome MC 8080
 CN Dioctadecanoyl phosphatidylcholine
 CN Dioctadecanoyllecithin
 CN Distearoyl-DL- α -phosphatidylcholine
 CN Distearoyl-DL-phosphatidylcholine
 CN Distearoyllecithin
 CN Distearoylphosphatidylcholine
 CN DL- α -Distearoyllecithin
 CN DSPC
 FS 3D CONCORD
 DR 816-93-3, 159022-80-7, 107041-14-5, 201412-81-9
 MF C44 H88 N 08 P
 CI COM
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
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 RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

CN Dipalmitoylphosphatidylcholine
CN Dipalmitoylphosphocholine
CN DL- α -DPPC
CN DL- β , γ -Dipalmitoyl- α -lecithin
CN DL- β , γ -Dipalmitoyl- α -phosphatidylcholine
CN dl-1,2-Dipalmitoyl-3-phosphatidylcholine
CN DL-3-Dipalmitoylphosphatidylcholine
CN DL-Dipalmitoyl- α -lecithin
CN DL-Dipalmitoyl- α -phosphatidylcholine
CN DL-Dipalmitoyllecithin
CN DL-Dipalmitoylphosphatidylcholine
CN DPPC
CN DPPC (phosphatide)
CN rac-1,2-Dipalmitoylglycerol-3-phosphorylcholine
CN rac-1,2-Dipalmitoylphosphatidylcholine
FS 3D CONCORD
DR 159022-81-8, 173839-68-4, 2797-68-4, 67118-46-1, 36441-53-9, 82623-33-4,

90289-55-7, 107041-15-6, 215369-06-5
MF C40 H80 N O8 P
CI COM
LC STN Files: ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB,
IPA, MEDLINE, NIOSHTIC, PIRA, PROMT, SPECINFO, TOXCENTER, USPAT2,
USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent;
Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
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RACT (Reactant or reagent); USES (Uses)
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study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP
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study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU
(Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT
(Reactant or reagent); USES (Uses); NORL (No role in record)
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(Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process);
PRP (Properties); RACT (Reactant or reagent)



6032 REFERENCES IN FILE CA (1907 TO DATE)
 69 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 6038 REFERENCES IN FILE CAPLUS (1907 TO DATE)
 16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
 RN 2462-63-7 REGISTRY
 CN 9-Octadecenoic acid γ (9Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl
]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 9-Octadecenoic acid (Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl
]-1,2-ethanediyl ester
 CN Ethanol, 2-amino-, dihydrogen phosphate (ester), monoester with
 1,2-diolein (8CI)
 CN Olein, 1,2-di-, 2-aminoethyl hydrogen phosphate (8CI)
 CN Olein, 1,2-di-, dihydrogen phosphate, 2-aminoethyl ester (7CI)
 CN Olein, 1,2-di-, phosphate, 2-aminoethyl ester (6CI)
 OTHER NAMES:
 CN 1,2-Dioleoyl phosphatidyl ethanolamine
 CN Dioleoyl (glycerophospho)ethanolamine
 CN Dioleoyl phosphatidylethanolamine
 CN DL-Dioleoylphosphatidylethanolamine
 CN DOPE
 CN LipofectACE
 FS STEREOSEARCH
 DR 159317-98-3, 5683-54-5
 MF C41 H78 N O8 P
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 LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
 CANCERLIT, CAOLD, CAPLUS, CSCHEM, EMBASE, IPA, MEDLINE, PROMT,
 TOXCENTER, USPAT2, USPATFULL
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 RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
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 (Properties); USES (Uses)

Double bond geometry as shown.

IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report

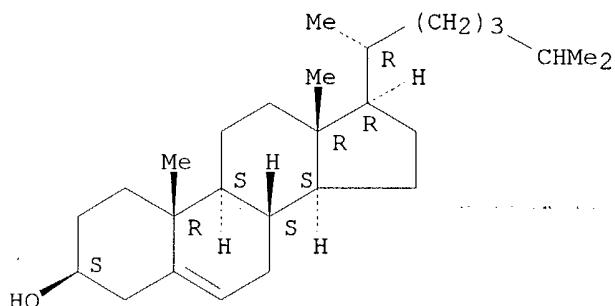
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

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Absolute stereochemistry



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

104023 REFERENCES IN FILE CA (1907 TO DATE)

8887 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

104207 REFERENCES IN FILE CAPLUS (1907 TO DATE)

15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)



linked to a moiety made of groups to which the species requirement has been applied.

Since all of the alternatives possess a common significant structural element and all of the combinations have the same utility, it is respectfully submitted that unity is present. Withdrawal of the species requirement is therefore respectfully solicited.

In an attempt to be complete, applicants advise the Examiner as follows.

With respect to species requirement 1, applicants select the species where Y is O, and for species requirement 2, applicants select the species where X^2 is N or P when m is 3; if a requirement is made to select within this group, applicants select nitrogen. With respect to the species requirement 3, of the species of R^8 listed in claim 21 applicants select C_{1-8} alkyl. In response to species group 4, applicants select R^5 being a bond, and with regard to the species group designated 5, applicants select the species where X^1 is N or P when n is 3, and if required to select further, applicants would select nitrogen. As to species group 6, of the species of R^6 listed in claim 22, applicant select C_{1-8} alkyl. Finally, with regard to species group 7, applicants select the first listed species in claim 32, namely distearoylphosphatidylcholine.

Applicants believe that all of the instant claims read on the elected species, however defined, other than claims 33 and 48.

the Patent Office is authorized to charge the underpayment to Deposit Account No. 04-1073.

AMENDMENTS

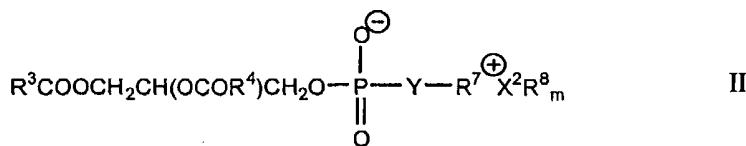
In the Claims:

Please cancel claim 1 without prejudice.

Please add new claims 21-49 pursuant to 37 C.F.R. § 1.121(c)(1)(i) as set forth in the "clean" version set forth below. Entry is respectfully requested.

21(NEW). An oral vaccine comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components and comprising

- a) at least one cationic compound;
- b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



in which R^3 and R^4 are the same or different and are a group of the formula $\text{CH}_3(\text{CH}_2)_e(\text{CH}=\text{CH}-\text{CH}_2)_f(\text{CH}_2)_g-$ in which f is 0 to 6, each of e and g are 0 to 23 and $e+g$ and $3f$ is in the range 12 to 23;

R^7 is a C_{1-8} alkanediyl group;

Y is $-\text{O}-$ or a bond;

X^2 is N, P or S;

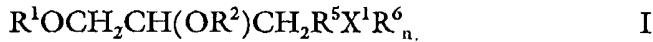
m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R⁸ are the same or different and are selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₆₋₁₁ aryl or aralkyl, or two or three of the groups R⁸ together with X² form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms,

in which at least 50% by mole of groups R³ and R⁴ has a value for f of 0 and which comprises a compound in which R³ and R⁴ are the same and have a value for f of 0:

in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

22(NEW). A vaccine according to claim 21 in which the cationic compound has the general formula I,



in which R¹ and R² are the same or different and are a group of the formula CH₃(CH₂)_a(CH=CH-CH₂)_b(CH₂)_c(CO)_d- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R⁵ is a bond or a C₁₋₈ alkanediyl group;

X¹ is N, P or S;

n is 3 where X¹ is N or P and is 2 where X¹ is S; and

the groups R⁶ are the same or different and are selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₆₋₁₂ aryl and aralkyl, or two or three of the groups R⁶ together with X¹ form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

23(NEW). A vaccine according to claim 22 in which R¹ is the same as R² and R³ is the same as R⁴.

24(NEW). A vaccine according to claim 23 in which R¹ and R² represent a different group to R³ and R⁴.

25(NEW). A vaccine according to claim 23 in which R¹ and R² represent a different group to R³ and R⁴, and in which in R¹ and R², b is 1, and in which (a + c) is in

the range 10 to 20.

26(NEW). A vaccine according to claim 23 in which d is 0.

27(NEW). A vaccine according to claim 22 in which X¹ is N and in which the R⁶ groups are all C₁₋₄ alkyl.

28(NEW). A vaccine according to claim 21 which comprises two zwitterionic phospholipids in each of which Y is O, X² is N, and the groups R⁸ of the first phospholipid are all hydrogen and the groups R⁸ of the second phospholipid are all C₁₋₄ alkyl.

29(NEW). A vaccine according to claim 28 in which, in each phospholipid R⁷ is (CH₂)_h in which h is 2 or 3.

30(NEW). A vaccine according to claim 28 in which the groups R³ and R⁴ of the said first phospholipid are the same and each is a group in which f is 1 and (e + g) is in the range 10 to 20.

31(NEW). A vaccine according to claim 30 in which in the groups R³ and R⁴ of the said second phospholipid are the same, f is O and e + g is in the range 15 to 23.

32(NEW). A vaccine according to claim 31 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, dipalmitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

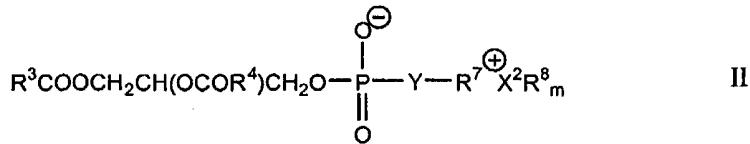
33(NEW). A vaccine according to claim 21 in which the cationic compound is cholesterol-3β-N-(dimethylaminoethyl) carbamate.

34(NEW). An oral vaccine according to claim 21 in which the liposome forming components include at least 25 mole% of components which individually have a transition temperature of more than 40°C.

35(NEW). A vaccine according to claim 21 in which the nucleic acid is entrapped within the liposomes.

36(NEW). A method of entrapping polynucleotide into liposomes involving the steps of:

- i) forming an aqueous suspension comprising naked nucleic acid, which operatively encodes an immunogenic polypeptide useful to induce a desired immune response in a human or animal subject, and preformed liposomes formed of liposome forming components comprising
 - a) at least one cationic compound;
 - b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



in which R^3 and R^4 are the same or different and are selected from groups of the formula $\text{CH}_3(\text{CH}_2)_e(\text{CH}=\text{CH-CH}_2)_f(\text{CH}_2)_g$ in which f is 0 to 6, each of e and g are 0 to 23 and $e + g$ and $3f$ is in the range 12 to 23;

R^7 is a C_{1-8} alkanediyl group;

Y is $-\text{O}-$ or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^2

form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms, in which at least 50% by mole of groups R³ and R⁴ has a value for f of 0 and which comprises a compound in which R³ and R⁴ are the same and have a value for f of 0: in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

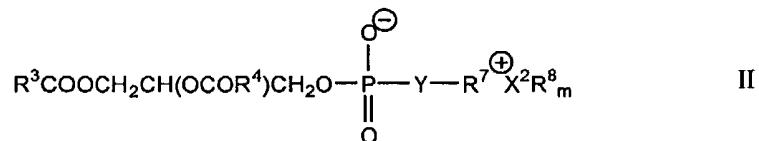
- ii) freeze-drying or spray-drying the suspension, and
- iii) rehydrating the product of step ii) to form dehydration/rehydration vesicles.

37(NEW). A method according to claim 36 comprising the further steps of:

- iv) subjecting the aqueous suspension of dehydration/rehydration vesicles from step iii to microfluidization to control their size; and
- v) optionally separating non-entrapped nucleic acid from liposomes.

38(NEW). Method of vaccinating an animal comprising administering orally a composition comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components comprising

- a) at least one cationic compound
- b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



in which R³ and R⁴ are the same or different and are a group of the formula $\text{CH}_3(\text{CH}_2)_e(\text{CH}=\text{CH-CH}_2)_g-$ in which f is 0 to 6, each of e and g + 3f are 0 to 23 and e + g is in the range 12 to 23;

R⁷ is a C₁₋₈ alkanediyl group;

Y is -O- or a bond;

X² is N, P or S;

m is 3 when X² is N or P and is 2 when X² is S; and

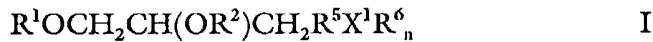
the groups R⁸ are the same or different and are selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₆₋₁₁ aryl or aralkyl, or two or three of the groups R⁸ together with X² form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms;

in which at least 50% by mole of groups R³ and R⁴ has a value for f of 0 and which comprises a compound in which R³ and R⁴ are the same and have a value for f of 0,

wherein the molar ratio of cationic compound to zwitterionic phospholipid is in the range 1:1 to 1:10,

whereby an immune response to the said antigen is generated.

40(NEW). A method according to claim 38 in which the cationic compound has the general formula I,



in which R¹ and R² are the same or different and are a group of the formula CH₃(CH₂)_a(CH=CH-CH₂)_b(CH₂)_c(CO)_d- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R⁵ is a bond or a C₁₋₈ alkanediyl group;

X¹ is N, P or S;

n is 3 where X¹ is N or P and is 2 where X¹ is S; and

the groups R⁶ are the same or different and are selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₆₋₁₂ aryl and aralkyl, or two or three of the groups R⁶ together with X¹ form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

41(NEW). A method according to claim 40 in which R¹ is the same as R² and R³ is the same as R⁴.

42(NEW). A method according to claim 41 in which R¹ and R² represent a

different group to R³ and R⁴.

43(NEW). A method according to claim 41 in which R¹ and R² represent a different group to R³ and R⁴, in which in R¹ and R², b is 1, and in which (a + c) is in the range 10 to 20.

44(NEW). A method according to claim 38 in which the liposome forming materials comprise two zwitterionic phospholipids in each of which Y is O, X² is N, and the groups R⁸ of the first phospholipid are all hydrogen and the groups R⁸ of the second phospholipid are all C₁₋₁₄ alkyl, and R⁷ is (CH₂)_h in which h is 2 or 3.

45(NEW). A method according to claim 44 in which the groups R³ and R⁴ of the said first phospholipid are the same and each is a group in which f is 1 and (e + g) is in the range 10 to 20.

46(NEW). A method according to claim 45 in which in the groups R³ and R⁴ of the said second phospholipid are the same f is 0 and e + g is in the range 15 to 23.

47(NEW). A method according to claim 46 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

48(NEW). A method according to claim 38 in which the cationic compound is cholesterol-3 β -N-(dimethyaminoethyl) carbamate.

49(NEW). A method according to claim 38 in which the nucleic acid is entrapped within the liposomes.